Figure 1a

Nucleic acid and amino acid sequence of TTXi DRG sodium channel

```
      tagcttgcttctgctaatgctaccccaggcctttagacagagaacagatggcagatggag
   1  ---------+---------+---------+---------+---------+---------+ 60
      atcgaacgaagacgattacgatggggtccggaaatctgtctcttgtctaccgtctacctc


      tttcttattgccatgcgcaaacgctgagcccacctcatgatcccggaccccatggttttc
  61  ---------+---------+---------+---------+----:----+---------+
      aaagaataacggtacgcgtttgcgactcgggtggagtactagggcctggggtaccaaaag


      agtagacaacctgggctaagaagagatctccgaccttatagagcagcaaagagtgtaaat
 121  ---------+---------+---------+---------+---------+---------+
      tcatctgttggacccgattcttctctagaggctggaatatctcgtcgtttctcacattta


      tcttccccaagaagaatgagaagATGGAGCTCCCCTTTGCGTCCGTGGGAACTACCAATT
 181  ---------+---------+---------+---------+---------+---------+
      agaaggggttcttcttactcttcTACCTCGAGGGGAAACGCAGGCACCCTTGATGGTTAA

                           M   E   L   P   F   A   S   V   G   T   T   N   F -

      TCAGACGGTTCACTCCAGAGTCACTGGCAGAGATCGAGAAGCAGATTGCTGCTCACCGCG
 241  ---------+---------+---------+-:-------+---------+---------+
      AGTCTGCCAAGTGAGGTCTCAGTGACCGTCTCTAGCTCTTCGTCTAACGACGAGTGGCGC

        R   R   F   T   P   E   S   L   A   E   I   E   K   Q   I   A   A   H   R   A -

      CAGCCAAGAAGGCCAGAACCAAGCACAGAGGACAGGAGGACAAGGGCGAGAAGCCCAGGC
 301  ---------+---------+---------+---------+---------+---------+
      GTCGGTTCTTCCGGTCTTGGTTCGTGTCTCCTGTCCTCCTGTTCCCGCTCTTCGGGTCCG

        A   K   K   A   R   T   K   H   R   G   Q   E   D   K   G   E   K   P   R   P -

      CTCAGCTGGACTTGAAAGACTGTAACCAGCTGCCCAAGTTCTATGGTGAGCTCCCAGCAG

 361  ---------+---------+---------+---------+---------+---------+
      GAGTCGACCTGAACTTTCTGACATTGGTCGACGGGTTCAAGATACCACTCGAGGGTCGTC

        Q   L   D   L   K   D   C   N   Q   L   P   K   F   Y   G   E   L   P   A   E -

      AACTGGTCGGGGAGCCCCTGGAGGACCTAGACCCTTTCTACAGCACACACCGGACATTCA
 421  ---------+---------+---------+---------+---------+---------+
      TTGACCAGCCCCTCGGGGACCTCCTGGATCTGGGAAAGATGTCGTGTGTGGCCTGTAAGT

          L   V   G   E   P   L   E   D   L   D   P   F   Y   S   T   H   R   T   F   M -

      TGGTGTTGAATAAAAGCAGGACCATTTCCAGATTCAGTGCCACTTGGGCCCTGTGGCTCT
 481  ---------+---------+---------+---------+---------+---------+
      ACCACAACTTATTTTCGTCCTGGTAAAGGTCTAAGTCACGGTGAACCCGGGACACCGAGA

          V   L   N   K   S   R   T   I   S   R   F   S   A   T   W   A   L   W   L   F -
```

```
     TCAGTCCCTTCAACCTGATCAGAAGAACAGCCATCAAAGTGTCTGTCCATTCCTGGTTCT
541  ---------+---------+---------+---------+---------+---------+
     AGTCAGGGAAGTTGGACTAGTCTTCTTGTCGGTAGTTTCACAGACAGGTAAGGACCAAGA

       S   P   F   N   L   I   R   R   T   A   I   K   V   S   V   H   S   W   F   S -


     CCATATTCATCACCATCACTATTTTGGTCAACTGCGTGTGCATGACCCGAACTGATCTTC
601  ---------+---------+---------+---------+---------+---------+
     GGTATAAGTAGTGGTAGTGATAAAACCAGTTGACGCACACGTACTGGGCTTGACTAGAAG

       I   F   I   T   I   T   I   L   V   N   C   V   C   M   T   R   T   D   L   P -

     CAGAGAAAGTCGAGTACGTCTTCACTGTCATTTACACCTTCGAGGCTCTGATTAAGATAC
661  ---------+---------+---------+---------+---------+---------+
     GTCTCTTTCAGCTCATGCAGAAGTGACAGTAAATGTGGAAGCTCCGAGACTAATTCTATG

       E   K   V   E   Y   V   F   T   V   I   Y   T   F   E   A   L   I   K   I   L -

     TGGCAAGAGGGTTTTGTCTAAATGAGTTCACTTATCTTCGAGATCCGTGGAACTGGCTGG
721  ---------+---------+---------+---------+---------+---------+
     ACCGTTCTCCCAAAACAGATTTACTCAAGTGAATAGAAGCTCTAGGCACCTTGACCGACC

       A   R   G   F   C   L   N   E   F   T   Y   L   R   D   P   W   N   W   L   D -

     ACTTCAGTGTCATTACCTTGGCGTATGTGGGTGCAGCGATAGACCTCCGAGGAATCTCAG
781  ---------+---------+---------+---------+---------+---------+
     TGAAGTCACAGTAATGGAACCGCATACACCCACGTCGCTATCTGGAGGCTCCTTAGAGTC

       F   S   V   I   T   L   A   Y   V   G   A   A   I   D   L   R   G   I   S   G -

     GCCTGCGGACATTCCGAGttctcagagccctgaaaactgtttctgtgatcccaggactga
841  ---------+---------+---------+---------+---------+---------+
     CGGACGCCTGTAAGGCTCaagagtctcgggacttttgacaaagacactagggtcctgact

       L   R   T   F   R   V   L   R   A   L   K   T   V   S   V   I   P   G   L   K -

     aggtcatcgtgggagccctgatccactcagtgaggaagctggccgacgtgactatcctca
901  ---------+---------+---------+---------+---------+---------+
     tccagtagcaccctcgggactaggtgagtcactccttcgaccggctgcactgataggagt

       V   I   V   G   A   L   I   H   S   V   R   K   L   A   D   V   T   I   L   T -

     cagtcttctgcctgagcgtcttcgccttggtgggcctgcagctctttaaggggaacctta
961  ---------+---------+---------+---------+---------+---------+
     gtcagaagacggactcgcagaagcggaaccacccggacgtcgagaaattcccctggaat

       V   F   C   L   S   V   F   A   L   V   G   L   Q   L   F   K   G   N   L   K -

     agaacaaatgcatcaggaacggaacagatccccacaaggctgacaacctctcatctgaaa
1021 ---------+---------+---------+---------+---------+---------+
     tcttgtttacgtagtccttgccttgtctaggggtgttccgactgttggagagtagacttt

       N   K   C   I   R   N   G   T   D   P   H   K   A   D   N   L   S   S   E   M -

     tggcagaatacgtctccatcaagcctggtactacggatcccttactgtgcggcaatgggt
1081 ---------+---------+---------+---------+---------+---------+
     accgtcttatgcagaggtagttcggaccatgatgcctagggaatgacacgccgttaccca

       A   E   Y   V   S   I   K   P   G   T   T   D   P   L   L   C   G   N   G   S -
```

```
         ctgatgctggtcactgccctggaggctatgtctgcctgaaaactcctgacaacccggatt
1141     ---------+---------+---------+---------+---------+---------+
         gactacgaccagtgacgggacctccgatacagacggacttttgaggactgttgggcctaa

          D   A   G   H   C   P   G   G   Y   V   C   L   K   T   P   D   N   P   D   F -


         ttaactacaccagctttgattcctttgcgtgggcattcctctcactgttccgcctcatga
1201     ---------+---------+---------+---------+---------+---------+
         aattgatgtggtcgaaactaaggaaacgcacccgtaaggagagtgacaaggcggagtact

          N   Y   T   S   F   D   S   F   A   W   A   F   L   S   L   F   R   L   M   T -


         cgcaggactcctgggagcgcctgtaccagcagacactccgggcttctgggaaaatgtaca
1261     ---------+---------+---------+---------+---------+---------+
         gcgtcctgaggaccctcgcggacatggtcgtctgtgaggcccgaagacctttttacatgt

          Q   D   S   W   E   R   L   Y   Q   Q   T   L   R   A   S   G   K   M   Y   M -

         tggtcttttttcgtgctggttattttccttggatcgttctacctggtcaatttgatcttgg
1321     ---------+---------+---------+---------+---------+---------+
         accagaaaaagcacgaccaataaaaggaacctagcaagatggaccagttaaactagaacc

          V   F   F   V   L   V   I   F   L   G   S   F   Y   L   V   N   L   I   L   A -

         ccgtggtcaccatggcgtatgaagagcagagccaggcaacaattgcagaaatcgaagcca
1381     ---------+---------+---------+---------+---------+---------+
         ggcaccagtggtaccgcatacttctcgtctcggtccgttgttaacgtctttagcttcggt

          V   V   T   M   A   Y   E   E   Q   S   Q   A   T   I   A   E   I   E   A   K -

         aggaaaaaaagttccaggaagcccttgaggtgctgcagaaggaacaggaggtgctggcag
1441     ---------+---------+---------+---------+---------+---------+
         tccttttttttcaaggtccttcgggaactccacgacgtcttccttgtcctccacgaccgtc

          E   K   K   F   Q   E   A   L   E   V   L   Q   K   E   Q   E   V   L   A   A -

         ccctggggattgacacgacctcgctccagtcccacagtggatcacccttagcctccaaaa
1501     ---------+---------+---------+---------+---------+---------+
         gggacccctaactgtgctggagcgaggtcagggtgtcacctagtgggaatcggaggtttt

          L   G   I   D   T   T   S   L   Q   S   H   S   G   S   P   L   A   S   K   N -

         acgccaatgagagaagacccagggtgaaatcaagggtgtcagagggctccacggatgaca
1561     ---------+---------+---------+---------+---------+---------+
         tgcggttactctcttctgggtcccactttagttcccacagtctcccgaggtgcctactgt

          A   N   E   R   R   P   R   V   K   S   R   V   S   E   G   S   T   D   D   N -

         acaggtcaccccaatctgacccttacaaccagcgcaggatgtctttcctaggcctgtctt
1621     ---------+---------+---------+---------+---------+---------+
         tgtccagtggggttagactgggaatgttggtcgcgtcctacagaaaggatccggacagaa

          R   S   P   Q   S   D   P   Y   N   Q   R   R   M   S   F   L   G   L   S   S -

         caggaagacgcagggctagccacggcagtgtgttccacttccgagcgcccagccaagaca
1681     ---------+---------+---------+---------+---------+---------+
         gtccttctgcgtcccgatcggtgccgtcacacaaggtgaaggctcgcgggtcggttctgt

          G   R   R   R   A   S   H   G   S   V   F   H   F   R   A   P   S   Q   D   I -
```

```
        tctcatttcctgacgggatcacccctgatgatggggtctttcacggagaccaggaaagcc
1741    ---------+---------+---------+---------+---------+---------+
        agagtaaaggactgccctagtggggactactaccccagaaagtgcctctggtcctttcgg

          S   F   P   D   G   I   T   P   D   D   G   V   F   H   G   D   Q   E   S   R  -

        gtcgaggttccatattgctgggcaggggtgctgggcagacaggtccactccccaggagcc
1801    ---------+---------+---------+---------+---------+---------+
        cagctccaaggtataacgacccgtccccacgacccgtctgtccaggtgaggggtcctcgg

          R   G   S   I   L   L   G   R   A   G   Q   T   G   P   L   P   R   S   P  -

        cactgcctcagtcccccaaccctggccgtagacatggagaagagggacagctcggagtgc
1861    ---------+---------+---------+---------+---------+---------+
        gtgacggagtcagggggggttgggaccggcatctgtacctcttctccctgtcgagcctcacg

          L   P   Q   S   P   N   P   G   R   R   H   G   E   E   G   Q   L   G   V   P  -

        ccactggtgagcttaccgctggagcgcctgaaggcccggcactgcacactacagggcaga
1921    ---------+---------+---------+---------+---------+---------+
        ggtgaccactcgaatggcgacctcgcggacttccgggccgtgacgtgtgatgtcccgtct

          T   G   E   L   T   A   G   A   P   E   G   P   A   L   H   T   T   G   Q   K  -

        agagcttcctgtctgcgggctacttgaacgaacctttccgagcacagagggccatgagcg
1981    ---------+---------+---------+---------+---------+---------+
        tctcgaaggacagacgcccgatgaacttgcttggaaaggctcgtgtctcccggtactcgc

          S   F   L   S   A   G   Y   L   N   E   P   F   R   A   Q   R   A   M   S   V  -

        ttgtcagtatcatgacttctgtcattgaggagcttgaagagtctaagctgaagtgcccac
2041    ---------+---------+---------+---------+---------+---------+
        aacagtcatagtactgaagacagtaactcctcgaacttctcagattcgacttcacgggtg

          V   S   I   M   T   S   V   I   E   E   L   E   E   S   K   L   K   C   P   P  -

        cctgcttgatcagcttcgctcagaagtatctgatctgggagtgctgccccaagtggagga
2101    ---------+---------+---------+---------+---------+---------+
        ggacgaactagtcgaagcgagtcttcatagactagaccctcacgacggggttcacctcct

          C   L   I   S   F   A   Q   K   Y   L   I   W   E   C   C   P   K   W   R   K  -

        agttcaagatggcgctgttcgagctggtgactgacccccttcgcagagcttaccatcaccc
2161    ---------+---------+---------+---------+---------+---------+
        tcaagttctaccgcgacaagctcgaccactgactggggaagcgtctcgaatggtagtggg

          F   K   M   A   L   F   E   L   V   T   D   P   F   A   E   L   T   I   T   L  -

        tctgcatcgtggtgaacaccgtcttcatggccatggagcactaccccatgaccgatgcct
2221    ---------+---------+---------+---------+---------+---------+
        agacgtagcaccacttgtggcagaagtaccggtacctcgtgatggggtactggctacgga

          C   I   V   V   N   T   V   F   M   A   M   E   H   Y   P   M   T   D   A   F  -

        tcgatgccatgcttcaagccggcaacattgtcttcaccgtgttttttcacaatggagatgg
2281    ---------+---------+---------+---------+---------+---------+
        agctacggtacgaagttcggccgttgtaacagaagtggcacaaaaagtgttacctctacc

          D   A   M   L   Q   A   G   N   I   V   F   T   V   F   F   T   M   E   M   A  -
```

```
      ccttcaagatcattgccttcgacccctactattacttccagaagaagtggaatatcttcg
2341  ---------+---------+---------+---------+---------+---------+
      ggaagttctagtaacggaagctggggatgataatgaaggtcttcttcaccttatagaagc

       F  K  I  I  A  F  D  P  Y  Y  Y  F  Q  K  K  W  N  I  F  D -

      actgtgtcatcgtcaccgtgagccttctggagctgagtgcatccaagaagggcagcctgt
2401  ---------+---------+---------+---------+---------+---------+
      tgacacagtagcagtggcactcggaagacctcgactcacgtaggttcttcccgtcggaca

       C  V  I  V  T  V  S  L  L  E  L  S  A  S  K  K  G  S  L  S -

      ctgtgctccgtaccttacgcttgctgcgggtcttcaagctggccaagtcctggcccaccc
2461  ---------+---------+---------+---------+---------+---------+
      gacacgaggcatggaatgcgaacgacgcccagaagttcgaccggttcaggaccgggtggg

       V  L  R  T  L  R  L  L  R  V  F  K  L  A  K  S  W  P  T  L -

      tgaacaccctcatcaagatcatcgggaactcagtggggggccctgggcaacctgaccttta
2521  ---------+---------+---------+---------+---------+---------+
      acttgtgggagtagttctagtagcccttgagtcacccccgggacccgttggactggaaat

       N  T  L  I  K  I  I  G  N  S  V  G  A  L  G  N  L  T  F  I -

      tcctggccatcatcgtcttcatcttcgccctggtcggaaagcagcttctctcagaggact
2581  ---------+---------+---------+---------+---------+---------+
      aggaccggtagtagcagaagtagaagcgggaccagcctttcgtcgaagagagtctcctga

       L  A  I  I  V  F  I  F  A  L  V  G  K  Q  L  L  S  E  D  Y -

      acgggtgccgcaaggacggcgtctccgtgtggaacggcgagaagctccgctggcacatgt
2641  ---------+---------+---------+---------+---------+---------+
      tgcccacggcgttcctgccgcagaggcacaccttgccgctcttcgaggcgaccgtgtaca

       G  C  R  K  D  G  V  S  V  W  N  G  E  K  L  R  W  H  M  C -

      gtgacttcttccattccttcctggtcgtcttccgaatcctctgcggggagtggatcgaga
2701  ---------+---------+---------+---------+---------+---------+
      cactgaagaaggtaaggaaggaccagcagaaggcttaggagacgcccctcacctagctct

       D  F  F  H  S  F  L  V  V  F  R  I  L  C  G  E  W  I  E  N -

      acatgtgggtctgcatggaggtcagccagaaatccatctgcctcatcctcttcttgactg
2761  ---------+---------+---------+---------+---------+---------+
      tgtacacccagacgtacctccagtcggtctttaggtagacggagtaggagaagaactgac

       M  W  V  C  M  E  V  S  Q  K  S  I  C  L  I  L  F  L  T  V -

      tgatggtgctgggcaacctagtggtgctcaaccttttcatcgctttactgctgaactcct
2821  ---------+---------+---------+---------+---------+---------+
      actaccacgacccgttggatcaccacgagttggaaaagtagcgaaatgacgacttgagga

       M  V  L  G  N  L  V  V  L  N  L  F  I  A  L  L  L  N  S  F -

      tcagcgcggacaacctcacggctccagaggatgacgggggaggtgaacaacttgcagttag
2881  ---------+---------+---------+---------+---------+---------+
      agtcgcgcctgttggagtgccgaggtctcctactgcccctccacttgttgaacgtcaatc

       S  A  D  N  L  T  A  P  E  D  D  G  E  V  N  N  L  Q  L  A -

      cactggccaggatccaggtacttggccatcgggccagcagggccagcgccagttacatca
```

```
2941 ---------+---------+---------+---------+---------+---------+
     gtgaccggtcctaggtccatgaaccggtagcccggtcgtcccggtcgcggtcaatgtagt
       L   A   R   I   Q   V   L   G   H   R   A   S   R   A   S   A   S   Y   I   S -

     gcagccactgccgattccactggcccaaggtggagacccagctgggcatgaagccccac
3001 ---------+---------+---------+---------+---------+---------+
     cgtcggtgacggctaaggtgaccgggttccacctctgggtcgacccgtacttcgggggtg
       S   H   C   R   F   H   W   P   K   V   E   T   Q   L   G   M   K   P   P   L -

     tcaccagctcagaggccaagaaccacattgccactgatgctgtcagtgctgcagtgggga
3061 ---------+---------+---------+---------+---------+---------+
     agtggtcgagtctccggttcttggtgtaacggtgactacgacagtcacgacgtcacccct
       T   S   S   E   A   K   N   H   I   A   T   D   A   V   S   A   A   V   G   N -

     acctgacaaagccagctctcagtagccccaaggagaaccacggggacttcatcactgatc
3121 ---------+---------+---------+---------+---------+---------+
     tggactgtttcggtcgagagtcatcggggttcctcttggtgcccctgaagtagtgactag
       L   T   K   P   A   L   S   S   P   K   E   N   H   G   D   F   I   T   D   P -

     ccaacgtgtgggtctctgtgcccattgctgagggggaatctgacctcgacgagctcgagg
3181 ---------+---------+---------+---------+---------+---------+
     ggttgcacacccagagacacgggtaacgactcccccttagactggagctgctcgagctcc
       N   V   W   V   S   V   P   I   A   E   G   E   S   D   L   D   E   L   E   E -

     aagatatggagcaggcttcgcagagctcctggcaggaagaggaccccaagggacagcagg
3241 ---------+---------+---------+---------+---------+---------+
     ttctatacctcgtccgaagcgtctcgaggaccgtccttctcctgggggttccctgtcgtcc
       D   M   E   Q   A   S   Q   S   S   W   Q   E   E   D   P   K   G   Q   Q   E -

     agcagttgccacaagtccaaaagtgtgaaaaccaccaggcagccagaagcccagcctcca
3301 ---------+---------+---------+---------+---------+---------+
     tcgtcaacggtgttcaggtttttcacactttttggtggtccgtcggtcttcgggtcggaggt
       Q   L   P   Q   V   Q   K   C   E   N   H   Q   A   A   R   S   P   A   S   M -

     tgatgtcctctgaggacctggctccatacctgggtgagagctggaagaggaaggatagcc
3361 ---------+---------+---------+---------+---------+---------+
     actacaggagactcctggaccgaggtatggacccactctcgaccttctccttcctatcgg
       M   S   S   E   D   L   A   P   Y   L   G   E   S   W   K   R   K   D   S   P -

     ctcaggtccctgccgagggagtggatgacacgagctcctctgagggcagcacggtggact
3421 ---------+---------+---------+---------+---------+---------+
     gagtccagggacggctccctcacctactgtgctcgaggagactcccgtcgtgccacctga
       Q   V   P   A   E   G   V   D   D   T   S   S   S   E   G   S   T   V   D   C -

     gcccggacccagaggaaatcctgaggaagatccccgagctggcacatgacctggacgagc
3481 ---------+---------+---------+---------+---------+---------+
     cggcctgggtctcctttaggactccttctaggggctcgaccgtgtactggacctgctcg
       P   D   P   E   E   I   L   R   K   I   P   E   L   A   H   D   L   D   E   P -
```

```
      ccgatgactgtttcagagaaggctgcactcgccgctgtccctgctgcaacgtgaatacta
3541  ---------+---------+---------+---------+---------+---------+
      ggctactgacaaagtctcttccgacgtgagcggcgacagggacgacgttgcacttatgat

        D   D   C   F   R   E   G   C   T   R   R   C   P   C   C   N   V   N   T   S -

      gcaagtctccttgggccacaggctggcaggtgcgcaagacctgctaccgcatcgtggagc
3601  ---------+---------+---------+---------+---------+---------+
      cgttcagaggaacccggtgtccgaccgtccacgcgttctggacgatggcgtagcacctcg

        K   S   P   W   A   T   G   W   Q   V   R   K   T   C   Y   R   I   V   E   H -

      acagctggtttgagagtttcatcatcttcatgatcctgctcagcagtggagcgctggcct
3661  ---------+---------+---------+---------+---------+---------+
      tgtcgaccaaactctcaaagtagtagaagtactaggacgagtcgtcacctcgcgaccgga

        S   W   F   E   S   F   I   I   F   M   I   L   L   S   S   G   A   L   A   F -

      ttgaggataactacctggaagagaaaccccgagtgaagtccgtgctggagtacactgacc
3721  ---------+---------+---------+---------+---------+---------+
      aactcctattgatggaccttctctttggggctcacttcaggcacgacctcatgtgactgg

        E   D   N   Y   L   E   E   K   P   R   V   K   S   V   L   E   Y   T   D   R -

      gagtgttcaccttcatcttcgtctttgagatgctgctcaagtgggtagcctatggcttca
3781  ---------+---------+---------+---------+---------+---------+
      ctcacaagtggaagtagaagcagaaactctacgacgagttcacccatcggataccgaagt

        V   F   T   F   I   F   V   F   E   M   L   L   K   W   V   A   Y   G   F   K -

      aaaagtatttcaccaatgcctggtgctggctggacttcctcattgtgaacatctccctga
3841  ---------+---------+---------+---------+---------+---------+
      ttttcataaagtggttacggaccacgaccgacctgaaggagtaacacttgtagagggact

        K   Y   F   T   N   A   W   C   W   L   D   F   L   I   V   N   I   S   L   T -

      caagcctcatagcgaagatccttgagtattccgacgtggcgtccatcAAAGCCCTTCGGA
3901  ---------+---------+---------+---------+---------+---------+
      gttcggagtatcgcttctaggaactcataaggctgcaccgcaggtagTTTCGGGAAGCCT

        S   L   I   A   K   I   L   E   Y   S   D   V   A   S   I   K   A   L   R   T -

      CTCTCCGTGCCCTCCGACCGCTGCGGGCTCTGTCTCGATTCGAAGGCATGAGGGTAGTGG
3961  ---------+---------+---------+---------+---------+---------+
      GAGAGGCACGGGAGGCTGGCGACGCCCGAGACAGAGCTAAGCTTCCGTACTCCCATCACC

        L   R   A   L   R   P   L   R   A   L   S   R   F   E   G   M   R   V   V   V -

      TGGATGCCCTCGTGGGCGCCATCCCCTCCATCATGAACGTCCTCCTCGTCTGCCTCATCT
4021  ---------+---------+---------+---------+---------+---------+
      ACCTACGGGAGCACCCGCGGTAGGGGAGGTAGTACTTGCAGGAGGAGCAGACGGAGTAGA

        D   A   L   V   G   A   I   P   S   I   M   N   V   L   L   V   C   L   I   F -

      TCTGGCTCATCTTCAGCATCATGGGCGTGAACCTCTTCGCCGGGAAATTTTCGAAGTGCG
4081  ---------+---------+---------+---------+---------+---------+
      AGACCGAGTAGAAGTCGTAGTACCCGCACTTGGAGAAGCGGCCCTTTAAAAGCTTCACGC

        W   L   I   F   S   I   M   G   V   N   L   F   A   G   K   F   S   K   C   V -
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      TCGACACCAGAAATAACCCATTTTCCAACGTGAATTCGACGATGGTGAATAACAAGTCCG
4141  ---------+---------+---------+---------+---------+---------+
      AGCTGTGGTCTTTATTGGGTAAAAGGTTGCACTTAAGCTGCTACCACTTATTGTTCAGGC

         D  T  R  N  N  P  F  S  N  V  N  S  T  M  V  N  N  K  S  E -

      AGTGTCACAATCAAAACAGCACCGGCCACTTCTTCTGGGTCAACGTCAAAGTCAACTTCG
4201  ---------+---------+---------+---------+---------+---------+
      TCACAGTGTTAGTTTTGTCGTGGCCGGTGAAGAAGACCCAGTTGCAGTTTCAGTTGAAGC

         C  H  N  Q  N  S  T  G  H  F  F  W  V  N  V  K  V  N  F  D -

      ACAACGTCGCTATGGGCTACCTCGCACTTCTTCAGGTGGCAACCTTCAAAGGCTGGATGG
4261  ---------+---------+---------+---------+---------+---------+
      TGTTGCAGCGATACCCGATGGAGCGTGAAGAAGTCCACCGTTGGAAGTTTCCGACCTACC

         N  V  A  M  G  Y  L  A  L  L  Q  V  A  T  F  K  G  W  M  D -

      ACATAATGTATGCAGCTGTTGATTCCGGAGAGATCAACAGTCAGCCTAACTGGGAGAACA
4321  ---------+---------+---------+---------+---------+---------+
      TGTATTACATACGTCGACAACTAAGGCCTCTCTAGTTGTCAGTCGGATTGACCCTCTTGT

         I  M  Y  A  A  V  D  S  G  E  I  N  S  Q  P  N  W  E  N  N -

      ACTTGTACATGTACCTGTACTTCGTCGTTTTCATCATTTTCGGTGGCTTCTTCACGCTGA
4381  ---------+---------+---------+---------+---------+---------+
      TGAACATGTACATGGACATGAAGCAGCAAAAGTAGTAAAAGCCACCGAAGAAGTGCGACT

         L  Y  M  Y  L  Y  F  V  V  F  I  I  F  G  G  F  F  T  L  N -

      ATCTCTTTGTTGGGGTCATAATCGACAACTTCAACCAACAGAAAAAAAAAGCTAGGAGGCC
4441  ---------+---------+---------+---------+---------+---------+
      TAGAGAAACAACCCCAGTATTAGCTGTTGAAGTTGGTTGTCTTTTTTTTCGATCCTCCGG

         L  F  V  G  V  I  I  D  N  F  N  Q  Q  K  K  K  L  G  G  Q -

      AGGACATCTTCATGACAGAAGAGCAGAAGAAGTACTACAATGCCATGAAGAAGCTGGGCT
4501  ---------+---------+---------+---------+---------+---------+
      TCCTGTAGAAGTACTGTCTTCTCGTCTTCTTCATGATGTTACGGTACTTCTTCGACCCGA

         D  I  F  M  T  E  E  Q  K  K  Y  Y  N  A  M  K  K  L  G  S -

      CCAAGAAACCCCAGAAGCCCATCCCACGGCCCCTGAATAAGTACCAAGGCTTCGTGTTTG
4561  ---------+---------+---------+---------+---------+---------+
      GGTTCTTTGGGGTCTTCGGGTAGGGTGCCGGGGACTTATTCATGGTTCCGAAGCACAAAC

         K  K  P  Q  K  P  I  P  R  P  L  N  K  Y  Q  G  F  V  F  D -

      ACATCGTGACCAGGCAAGCCTTTGACATCATCATCATGGTTCTCATCTGCCTCAACATGA
4621  ---------+---------+---------+---------+---------+---------+
      TGTAGCACTGGTCCGTTCGGAAACTGTAGTAGTAGTACCAAGAGTAGACGGAGTTGTACT

         I  V  T  R  Q  A  F  D  I  I  I  M  V  L  I  C  L  N  M  I -

      TCACCATGATGGTGGAGACCGACGAGCAGGGCGAGGAGAAGACGAAGGTTCTGGGCAGAA
4681  ---------+---------+---------+---------+---------+---------+
      AGTGGTACTACCACCTCTGGCTGCTCGTCCCGCTCCTCTTCTGCTTCCAAGACCCGTCTT

         T  M  M  V  E  T  D  E  Q  G  E  E  K  T  K  V  L  G  R  I -
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         TCAACCAGTTCTTTGTGGCCGTCTTCACGGGCGAGTGTGTGATGAAGATGTTCGCCCTGC
  4741   ---------+---------+---------+---------+---------+---------+
         AGTTGGTCAAGAAACACCGGCAGAAGTGCCCGCTCACACACTACTTCTACAAGCGGGACG

            N  Q  F  F  V  A  V  F  T  G  E  C  V  M  K  M  F  A  L  R -

         GACAGTACTACTTCACCAACGGCTGGAACGTGTTCGACTTCATAGTGGTGATCCTGTCCA
  4801   ---------+---------+---------+---------+---------+---------+
         CTGTCATGATGAAGTGGTTGCCGACCTTGCACAAGCTGAAGTATCACCACTAGGACAGGT

            Q  Y  Y  F  T  N  G  W  N  V  F  D  F  I  V  V  I  L  S  I -

         TTGGGAGTCTGCTGTTTTCTGCAATCCTTAAGTCACTGGAAAACTACTTCTCCCCGACGC
  4861   ---------+---------+---------+---------+---------+---------+
         AACCCTCAGACGACAAAAGACGTTAGGAATTCAGTGACCTTTTGATGAAGAGGGGCTGCG

            G  S  L  L  F  S  A  I  L  K  S  L  E  N  Y  F  S  P  T  L -

         TCTTCCGGGTCATCCGTCTGGCCAGGATCGGCCGCATCCTCAGGCTGATCCGAGCAGCCA
  4921   ---------+---------+---------+---------+---------+---------+
         AGAAGGCCCAGTAGGCAGACCGGTCCTAGCCGGCGTAGGAGTCCGACTAGGCTCGTCGGT

            F  R  V  I  R  L  A  R  I  G  R  I  L  R  L  I  R  A  A  K -

         AGGGGATTCGCACGCTGCTCTTCGCCCTCATGATGTCCCTGCCCGCCCTCTTCAACATCG
  4981   ---------+---------+---------+---------+---------+---------+
         TCCCCTAAGCGTGCGACGAGAAGCGGGAGTACTACAGGGACGGGCGGGAGAAGTTGTAGC

            G  I  R  T  L  L  F  A  L  M  M  S  L  P  A  L  F  N  I  G -

         GCCTCCTCCTCTTCCTCGTCATGTTCATCTACTCCATCTTCGGCATGGCCAGCTTCGCTA
  5041   ---------+---------+---------+---------+---------+---------+
         CGGAGGAGGAGAAGGAGCAGTACAAGTAGATGAGGTAGAAGCCGTACCGGTCGAAGCGAT

            L  L  L  F  L  V  M  F  I  Y  S  I  F  G  M  A  S  F  A  N -

         ACGTCGTGGACGAGGCCGGCATCGACGACATGTTCAACTTCAAGACCTTTGGCAACAGCA
  5101   ---------+---------+---------+---------+---------+---------+
         TGCAGCACCTGCTCCGGCCGTAGCTGCTGTACAAGTTGAAGTTCTGGAAACCGTTGTCGT

            V  V  D  E  A  G  I  D  D  M  F  N  F  K  T  F  G  N  S  M -

         TGCTGTGCCTGTTCCAGATCACCACCTCGGCCGGCTGGGACGGCCTCCTCAGCCCCATCC
  5161   ---------+---------+---------+---------+---------+---------+
         ACGACACGGACAAGGTCTAGTGGTGGAGCCGGCCGACCCTGCCGGAGGAGTCGGGGTAGG

            L  C  L  F  Q  I  T  T  S  A  G  W  D  G  L  L  S  P  I  L -

         TCAACACGGGGCCTCCCTACTGCGACCCCAACCTGCCCAACAGCAACGGCTCCCGGGGGA
  5221   ---------+---------+---------+---------+---------+---------+
         AGTTGTGCCCCGGAGGGATGACGCTGGGGTTGGACGGGTTGTCGTTGCCGAGGGCCCCCT

            N  T  G  P  P  Y  C  D  P  N  L  P  N  S  N  G  S  R  G  N -

         ACTGCGGGAGCCCGGCGGTGGGCATCATCTTCTTCACCACCTACATCATCATCTCCTTCC
  5281   ---------+---------+---------+---------+---------+---------+
         TGACGCCCTCGGGCCGCCACCCGTAGTAGAAGAAGTGGTGGATGTAGTAGTAGAGGAAGG

            C  G  S  P  A  V  G  I  I  F  F  T  T  Y  I  I  I  S  F  L -
```

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       TCATCGTGGTCAACATGTACATCGCAGTGATTCTGGAGAACTTCAACGTAGCCACCGAGG
5341   ---------+---------+---------+---------+---------+---------+
       AGTAGCACCAGTTGTACATGTAGCGTCACTAAGACCTCTTGAAGTTGCATCGGTGGCTCC

         I  V  V  N  M  Y  I  A  V  I  L  E  N  F  N  V  A  T  E  E -

       AGAGCACGGAGCCCCTGAGCGAGGACGACTTCGACATGTTCTATGAGACCTGGGAGAAGT
5401   ---------+---------+---------+---------+---------+---------+
       TCTCGTGCCTCGGGGACTCGCTCCTGCTGAAGCTGTACAAGATACTCTGGACCCTCTTCA

         S  T  E  P  L  S  E  D  D  F  D  M  F  Y  E  T  W  E  K  F -

       TCGACCCGGAGGCCACCCAGTTCATTGCCTTTTCTGCCCTCTCAGACTTCGCGGACACGC
5461   ---------+---------+---------+---------+---------+---------+
       AGCTGGGCCTCCGGTGGGTCAAGTAACGGAAAAGACGGGAGAGTCTGAAGCGCCTGTGCG

         D  P  E  A  T  Q  F  I  A  F  S  A  L  S  D  F  A  D  T  L -

       TCTCCGGCCCTCTTAGAATCCCCAAACCCAACCAGAATATATTAATCCAGATGGACCTGC
5521   ---------+---------+---------+---------+---------+---------+
       AGAGGCCGGGAGAATCTTAGGGGTTTGGGTTGGTCTTATATAATTAGGTCTACCTGGACG

         S  G  P  L  R  I  P  K  P  N  Q  N  I  L  I  Q  M  D  L  P -

       CGTTGGTCCCCGGGGATAAGATCCACTGTCTGGACATCCTTTTTGCCTTCACAAAGAACG
5581   ---------+---------+---------+---------+---------+---------+
       GCAACCAGGGGCCCCTATTCTAGGTGACAGACCTGTAGGAAAAACGGAAGTGTTTCTTGC

         L  V  P  G  D  K  I  H  C  L  D  I  L  F  A  F  T  K  N  V -

       TCTTGGGAGAATCCGGGGAGTTGGACTCCCTGAAGACCAATATGGAAGAGAAGTTTATGG
5641   ---------+---------+---------+---------+---------+---------+
       AGAACCCTCTTAGGCCCCTCAACCTGAGGGACTTCTGGTTATACCTTCTCTTCAAATACC

         L  G  E  S  G  E  L  D  S  L  K  T  N  M  E  E  K  F  M  A -

       CGACCAATCTCTCCAAAGCATCCTATGAACCAATAGCCACCACCCTCCGGTGGAAGCAGG
5701   ---------+---------+---------+---------+---------+---------+
       GCTGGTTAGAGAGGTTTCGTAGGATACTTGGTTATCGGTGGTGGGAGGCCACCTTCGTCC

         T  N  L  S  K  A  S  Y  E  P  I  A  T  T  L  R  W  K  Q  E -

       AAGACCTCTCAGCCACAGTCATTCAAAAGGCCTACCGGAGCTACATGCTGCACCGCTCCT
5761   ---------+---------+---------+---------+---------+---------+
       TTCTGGAGAGTCGGTGTCAGTAAGTTTTCCGGATGGCCTCGATGTACGACGTGGCGAGGA

         D  L  S  A  T  V  I  Q  K  A  Y  R  S  Y  M  L  H  R  S  L -

       TGACACTCTCCAACACCCTGCATGTGCCCAGGGCTGAGGAGGATGGCGTGTCACTTCCCG
5821   ---------+---------+---------+---------+---------+---------+
       ACTGTGAGAGGTTGTGGGACGTACACGGGTCCCGACTCCTCCTACCGCACAGTGAAGGGC

         T  L  S  N  T  L  H  V  P  R  A  E  E  D  G  V  S  L  P  G -

       GGGAAGGCTACATTACATTCATGGCAAACAGTGGACTCCCGGACAAATCAGAAACTGCCT
5881   ---------+---------+---------+---------+---------+---------+
       CCCTTCCGATGTAATGTAAGTACCGTTTGTCACCTGAGGGCCTGTTTAGTCTTTGACGGA

         E  G  Y  I  T  F  M  A  N  S  G  L  P  D  K  S  E  T  A  S -

       CTGCTACGTCTTTCCCGCCATCCTATGACAGTGTCACCAGGGGCCTGAGTGACCGGGCCA
```

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5941 ---------+---------+---------+---------+---------+---------+
     GACGATGCAGAAAGGGCGGTAGGATACTGTCACAGTGGTCCCCGGACTCACTGGCCCGGT

       A  T  S  F  P  P  S  Y  D  S  V  T  R  G  L  S  D  R  A  N -

     ACATTAACCCATCTAGCTCAATGCAAAATGAAGATGAGGTCGCTGCTAAGGAAGGAAACA
6001 ---------+---------+---------+---------+---------+---------+
     TGTAATTGGGTAGATCGAGTTACGTTTTACTTCTACTCCAGCGACGATTCCTTCCTTTGT


       I  N  P  S  S  S  M  Q  N  E  D  E  V  A  A  K  E  G  N  S -

     GCCCTGGACCTCAGTGAAGGCACTCAGGCATGCACAGGGCAGGTTCCAATGTCTTTCTCT
6061 ---------+---------+---------+---------+---------+---------+
     CGGGACCTGGAGTCACTTCCGTGAGTCCGTACGTGTCCCGTCCAAGGTTACAGAAAGAGA


       P  G  P  Q  *

     GCTGTACTAACTCCTTCCCTCTGGAGGTGGCACCAACCTCCAGCCTCCACCAATGCATGT
6121 ---------+---------+---------+---------+---------+---------+
     CGACATGATTGAGGAAGGGAGACCTCCACCGTGGTTGGAGGTCGGAGGTGGTTACGTACA


     CACTGGTCATGGTGTCAGAACTGAATGGGGACATCCTTGAGAAAGCCCCCACCCCAATAG
6181 ---------+---------+---------+---------+---------+---------+
     GTGACCAGTACCACAGTCTTGACTTACCCCTGTAGGAACTCTTTCGGGGGTGGGGTTATC


     GAATCAAAAGCCAAGGATACTCCTCCATTCTGACGTCCCTTCCGAGTTCCCAGAAGATGT
6241 ---------+---------+---------+---------+---------+---------+
     CTTAGTTTTCGGTTCCTATGAGGAGGTAAGACTGCAGGGAAGGCTCAAGGGTCTTCTACA


     CATTGCTCCCTTCTGTTTGTGACCAGAGACGTGATTCACCAACTTCTCGGAGCCAGAGAC
6301 ---------+---------+---------+---------+---------+---------+
     GTAACGAGGGAAGACAAACACTGGTCTCTGCACTAAGTGGTTGAAGAGCCTCGGTCTCTG


     ACATAGCAAAGACTTTTCTGCTGGTGTCGGGCAGTCTTAGAGAAGTCACGTAGGGGTTGG
6361 ---------+---------+---------+---------+---------+---------+
     TGTATCGTTTCTGAAAAGACGACCACAGCCCGTCAGAATCTCTTCAGTGCATCCCCAACC


     TACTGAGAATTAGGGTTTGCATGACTGCATGCTCACAGCTGCCGGACAATACCTGTGAGT
6421 ---------+---------+---------+---------+---------+---------+
     ATGACTCTTAATCCCAAACGTACTGACGTACGAGTGTCGACGGCCTGTTATGGACACTCA


     CGGCCATTAAAATTAATATTTTTAAAGTTAAAAAAAAAAAAAAAA
6481 ---------+---------+---------+---------+----  6524
     GCCGGTAATTTTAATTATAAAAATTTCAATTTTTTTTTTTTTTTT
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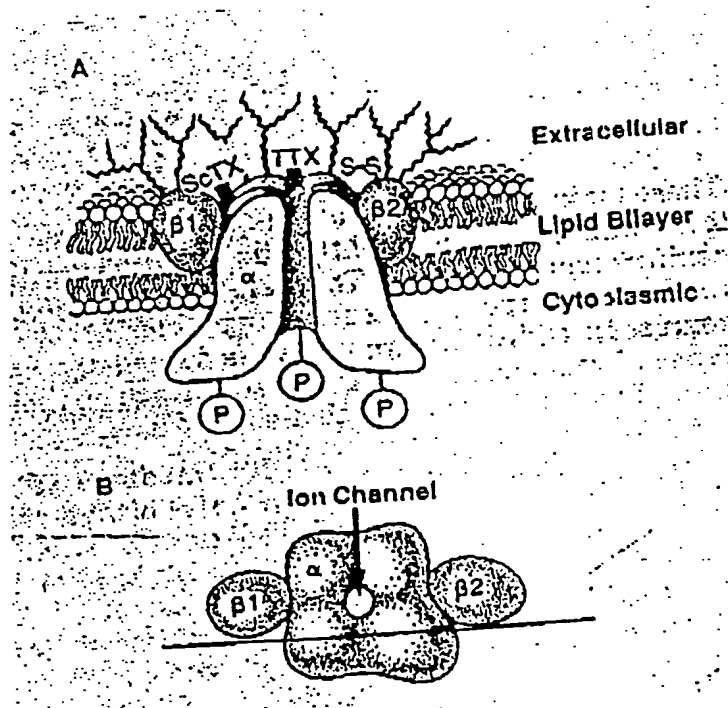
Figure 1b

Structure of SNS-B voltage-gated sodium channel in pGEM-3Z

SNS-B voltage gated sodium channel
PNC IB XOI- construct
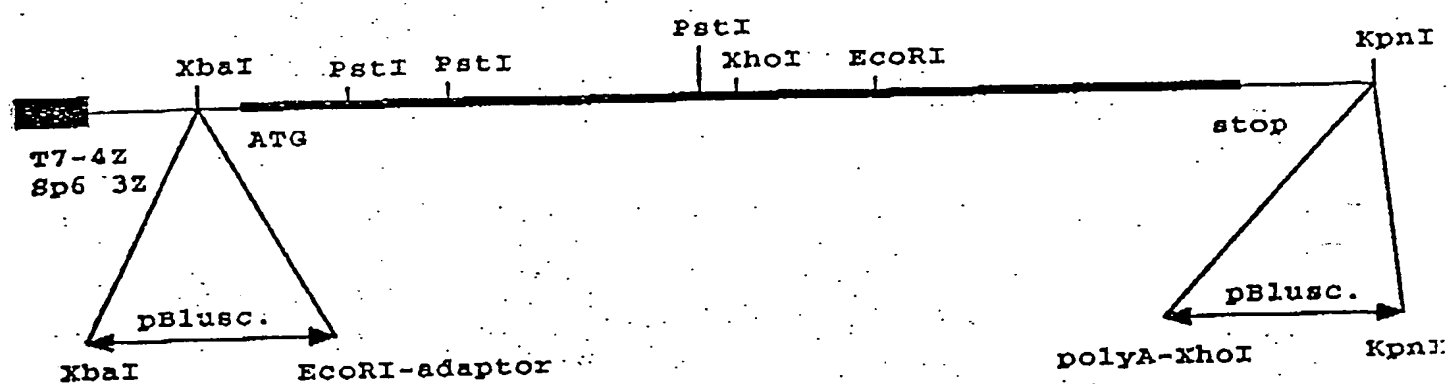
Constructs were generated in pGem 3z
nd pGem 4z with bluescript polylinkers
. Linearization site is KPNI

Figure 1c

Schematised drawing of voltage-gated sodium channel (from Caterall 1992)

FIGURE 2

Sequence of PCR primers for isolation of human clone probes

a) *Highly conserved regions of all sodium channels*

1) Position 2475-2510 S4 Domain II

Degenerate primers (20-24mers) encoding amino acid residues
RLLRVFKLAKSWPTL or non degenerate primers within this
region e.g. 5' gcttgctgcgggtcttcaagc 3'

2) Position 3961 - 4010 S4 Domain III

Degenerate primers encoding the complementary strand
encoding residues LRALPLRALSRFEG or non degenerate
primers within this region e.g. 5' atcgagacagagcccgcagcg 3'

b) *Unique sequence primers for SNS-homologues*
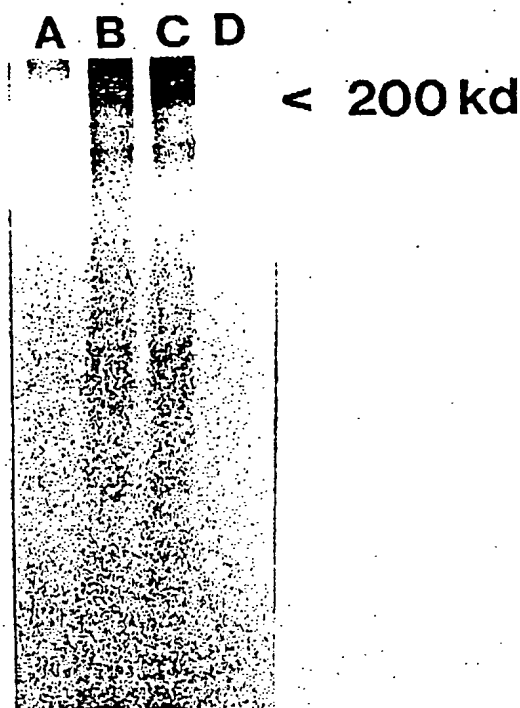
e.g. residues with the region 2641-2680

e.g. 5' acgggtgccgcaaggacggcgtctccgtgtggaacggcgagaag 3'

and complementary sequence within the region 3375 and 3420

e.g. 5' ggctatccttcctcttccagctctcacccaggtatggagccaggt 3'
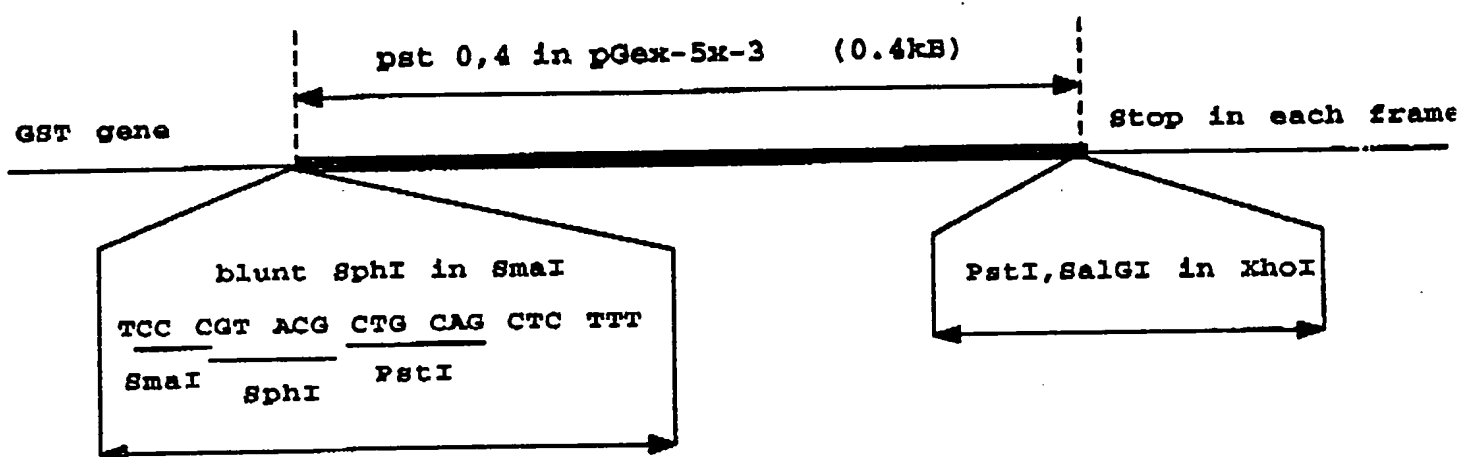
Figure 3

In vitro synthesis of S-35 methionine labelled SNS-B voltage gated sodium channel in a coupled transcription/translation system

Autoradiograph of a 7.5% SDS polyacrylamide gel, showing the migration of labelled proteins compared to the sizes of known molecular weight markers (Amersham rainbow markers). Lane A control, Lane B SNS-B, Lane C SNS-B, Lane D control. The predicted 200kDa band representing the SNS-B sodium channel is arrowed.

Figure 4a

D1-extracellular
construct for SNS antibody

pst 0,4 in pGex-5x-3   (0.4kB)

GST gene

Stop in each frame

blunt SphI in SmaI

TCC CGT ACG CTG CAG CTC TTT

SmaI SphI PstI

PstI,SalGI in XhoI

C-terminal (intracellular)
construct for antibody

SphI 0,9 (smaI-sphI 3'-end)

pGex-4T-2   (0,2kB)

GST gene

Stop in
NaCh insert

CCC GGG GAA GGC TAC

SmaI

SphI, PstI, SalGI
in XhoI
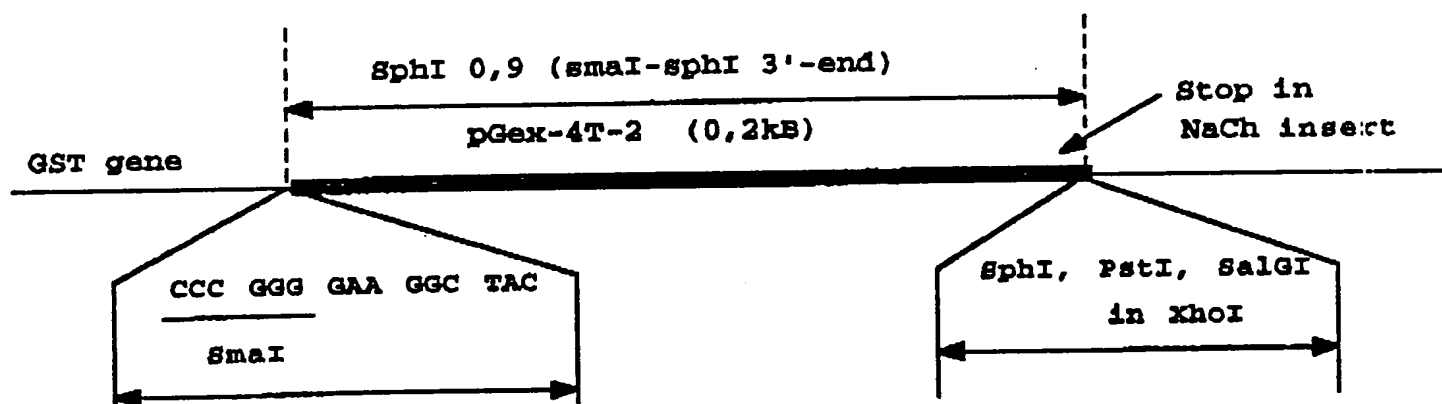
Figure 4b

Extracellular D3
construct for antibody

SalGI-PrA(NotI) from Bam-XhoI 3,3kB in

pGex-5X-3   (0,2kB)

Stop in each
frame

GST gene

GTC GAC   ACC AGA AAT

SalGI

PrA (NotI) in NotI
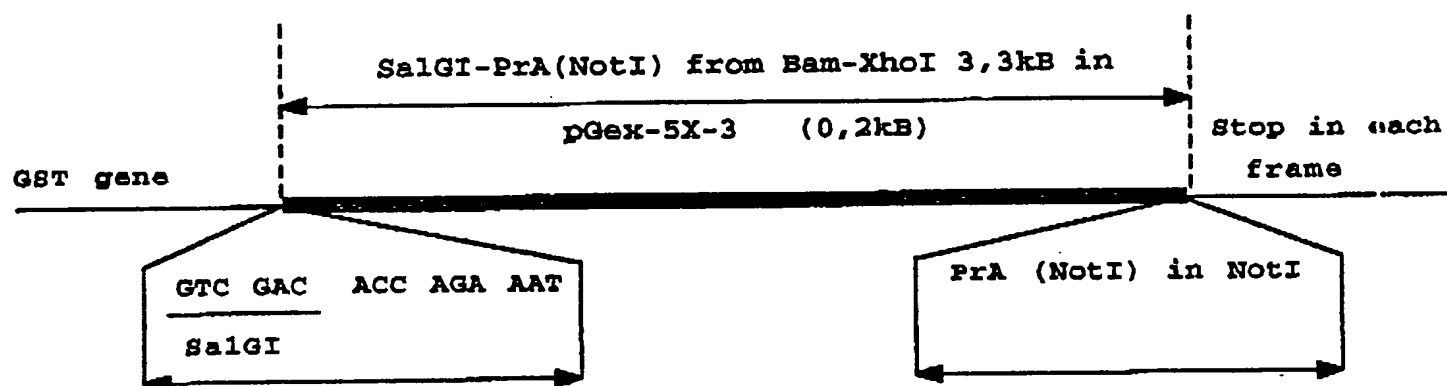
Intracellular D1-D2
construct for antibody

PstI-pr24 from PstI 1.7 in

pGex-4T-2   (0,45kB)

Stop in each frames

GST gene

GGA TCC TCT AGA GTC GAC CTG CAG AAG GAA

BamHI   XbaI   SalGI   PstI

pr24 in SmaI